ANTIDEPRESSANTS AND THE RISK OF SUICIDAL BEHAVIOR

Introduction

Research has indicated that early identification and comprehensive treatment of mental health disorders can significantly improve the prognosis for children. Clinical trials are being conducted to ascertain which treatments are the most successful in treating children and adolescents with mental health disorders. Many of these are outlined in the *Collection* and are highlighted in the *Collection*'s "Reference Chart of Disorders and Evidence-based Treatments." These evidence-based treatment modalities include cognitive-behavioral therapy, family therapy, group therapy, and pharmacological approaches, including the use of antidepressants. One major research finding, as indicated in previous studies, is that a combination of psychotherapy and antidepressant medication has been the most efficacious in treating depression in children and adolescents (March, Silva, Petrycki, as cited by Lock et al., 2005). Moreover, additional findings have revealed that antidepressant medication may have almost as much benefit as other treatments combined (March, Silva, Petrycki, as cited by Lock et al.).

While there are several different types of medications used for treating mental health disorders in children, this section will concentrate on the use of antidepressant medications by children and adolescents, as well as information both caregivers and clinicians need to know regarding the use of these medications.

Increases in the Use of Psychotropic Medications

In recent years, research has been conducted to review the patterns and effects of psychotropic medication use by children and adolescents. One such study conducted in the United States showed that the overall rate of psychotropic medication use by children has increased significantly in recent decades (Olfson, et al., 2002). Significant increases were found in the rate of stimulant use, antidepressant use, other psychotropic medications, and coprescription of different classes of medication, especially antidepressants and stimulants (Olfson, et al.). The common types of medications used for treating mental disorders are outlined in Table 1.

Table 1

Common Types of Psychotropic Medications

Stimulants are often used as part of treatment for attention deficit hyperactivity disorder (ADHD).

Antidepressants are used in the treatment of depression, school phobias, panic attacks, and other anxiety disorders, bed wetting, eating disorders, obsessive compulsive disorder, personality disorders, post-traumatic stress disorder, and ADHD. There are several types: tricyclics (TCAs); selective serotonin reuptake inhibitors (SSRIs); monoamine oxidase inhibitors (MAOIs); and atypical medications.

Antipsychotics can help control psychotic symptoms (delusions or hallucinations) or disorganized thinking. They may also help muscle twitches or verbal outbursts. Occasionally, they may be used to treat severe anxiety and may help reduce very aggressive behavior.

Mood Stabilizers and **Anticonvulsants** may help treat manic-depressive episodes, mood swings, aggressive behavior, impulse-control disorders and severe mood symptoms in schizophrenia.

Anti-anxiety medications can help treat severe anxiety. There are several types of anti-anxiety medications, including benzodiazepines, antihistamines, and atypical medications.

Source: American Academy of Child & Adolescent Psychiatry (AACAP), 2000.

Antidepressant use rapidly increased among adolescents, with use among very young children increasing at even faster rates (Delate, as cited by DeNoon, 2004). Analysis from pharmacy benefit management databases, as outlined by DeNoon for WebMD, has revealed the following:

- Child antidepressant use increased by 9.2% each year between 1998 and 2002.
- Antidepressant prescriptions increased faster for girls than for boys.
- Serotonin-specific reuptake inhibitors (SSRIs) were more commonly prescribed than other antidepressants.
- Data shows doctors prescribed antidepressants more frequently for depression than for anxiety disorders.

There are differing opinions about the increased use of antidepressants in children and adolescents, as discussed by Delate (DeNoon, 2004). One view is that antidepressants were being prescribed to youth without adequate information about their safety and efficacy in this population. A second viewpoint asserts that, in recent years, rigorous efforts to identify and aggressively treat depression in children and adolescents have caused this increase (DeNoon). Both perspectives point toward the need for greater study and analysis of the use of antidepressants among children and adolescents.

Food and Drug Administration Advisory Statement

In September 2004, the U.S. Food and Drug Administration (FDA) released a statement based on the recommendations of the Psychopharmacologic Drugs and Pediatric Advisory Committees regarding antidepressant use in pediatric patients (Wolf, 2005). The Advisory Committees concluded that there was an increased risk of suicidality in pediatric patients for all antidepressants in controlled pediatric antidepressant trials. In response to this concern, the FDA directed

manufacturers to add a black-box warning to the health professional label on antidepressants to describe the increased risk of suicidal thoughts and behavior in children and adolescents.

The FDA (2004) determined that the following points were to be included on the boxed warning:

- Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders.
- Anyone considering the use of an antidepressant in a child or adolescent for any clinical use must balance the risk of increased suicidality with the clinical need.
- Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.
- Families and caregivers should be advised to closely observe the patient and to communicate with the prescriber.
- A statement regarding whether the particular drug is approved for any pediatric indication(s) and, if so, which one(s).

The FDA warning instructs clinicians prescribing antidepressants to children to inform parents and custodial adults of the black-box warning about the increased risk of suicidality. While an advisory statement was issued, the Advisory Committees did have a split decision (15 yes, 8 no) regarding recommendations for a black-box warning for the increased risk of suicidality (Wolf, 2005). In response to this, some practitioners have ceased prescribing antidepressants to children and have begun to refer patients to child and adolescent psychiatrists (Virginia Joint Commission on Health Care, 2005). On May 2, 2007, the FDA expanded the black-box warning by incorporating information about an increased risk of suicidal symptoms in young adults 18 to 24 years of age (FDA, 2007).

Study Activities on Antidepressants and Suicidality

In response to the FDA's advisory statement, a study was conducted by researchers at the Injury Control Research Center at Harvard School of Public Health. The study revealed that 11% of 123 youth suicide completers and 21% of 2,674 adults who died by suicide tested positive for the presence of an antidepressant (Jancin, 2005). This study effort was conducted by obtaining data from the Centers for Disease Control and Prevention's National Violent Death Reporting System. The findings from this study indicated that: study subjects' sensitivity to toxicology tests may be low; patients who committed suicide may have received psychotherapy without medication; or the progress of these patients was not being carefully monitored (Jancin). Patient compliance to treatment and the need for improved case management were two findings cited in this study that must also be considered in evaluating patients risk for suicide (Jancin).

The following information is taken from the National Institute of Mental Health (NIMH) (2008). Researchers are evaluating the relationship between antidepressant medications and suicide, but study results are mixed. Findings from a comprehensive review of pediatric trials conducted between 1988 and 2006 suggest that the benefits of antidepressant medications likely outweigh their risks to children and adolescents with major depression and anxiety disorders (Bridge et al., 2007). Another study, using national Medicaid files, found in adults, the use of antidepressants did not seem to be related to suicide attempts or deaths. However, this analysis revealed that the use of antidepressant medications might be related to suicide attempts and deaths among children and adolescents (Olfson et al., 2006). Another study analyzed health plan records for 65,103 patients treated for depression. After starting treatment, there was no significant increase

in the risk for suicide with newer antidepressant medications (Simon et al., 2006). A third study analyzed suicide data from the National Vital Statistics and commercial prescription data. This study found that, among children ages five to 14, suicide rates from 1996 to 1998 were actually lower in areas of the country with higher rates of SSRI antidepressant prescriptions (Gibbons et al., 2006). The relationship between the suicide rates and the SSRI use rates remains unclear.

Responses to FDA Advisory

The American Medical Association (AMA) Council on Scientific Affairs responded to the FDA advisory by conducting a separate analysis and issued a statement to address the concerns raised by the FDA. Based on their preliminary analysis, the AMA asserted that antidepressants could be advantageous in treatment of depression in pediatric patients, but indicated that longer-term studies were needed to better address safety concerns (AMA, 2005). They requested the FDA to evaluate the black-box warning's impact on treatment patterns, patient compliance and patient access to the drugs.

According to the New York State Office of Mental Health (2004), researchers are currently analyzing all available information in order to provide families and clinicians with the most current information. However, they caution that the risks associated with not treating depression must be considered in all future activity. Failure or refusal to treat significant psychiatric disorder in children and adolescents, which may include reluctance to utilize medications, is a cause for concern (New York State Office of Mental Health).

Since the issuance of the advisory statement, antidepressant use among children declined by approximately 10% (Reuters Health Information, 2005). This occurrence was noted in the final quarter of 2004 by various pharmacy benefit firms.

Implications for Families

According to the New York State Office of Mental Health, families and physicians must carefully monitor a child for any behavioral changes if they are taking antidepressants (2004). The New York State Office of Mental Health has informed parents that, in most instances, the increased risk of suicidal behavior occurs during the first four to six weeks of treatment. Families must have careful dialogue with their child's physician if their child is being prescribed antidepressant medications. Discussion should include the possible benefits, as well as the possible risks, including increased suicidal behavior (New York State Office of Mental Health). Caregivers should proceed with caution if their child or adolescent is taking antidepressants. Table 2 outlines recommendations for families while their child or adolescent is taking antidepressants.

Cultural Considerations

The following observations are taken from a study conducted by Olfson, Marcus, Weissman, & Jensen (2002). The authors of this study noted that the increase in the use of psychotropic medication has been observed in all age, racial/ethnic, geographic, gender and insurance groups. While `1there has been an overall increase in antidepressant use in all children and adolescents, African-American children are somewhat less likely than Caucasian children to receive stimulants and antidepressants. This is despite lack of evidence supporting racial differences in prevalence of ADHD or childhood depression. Thus, the authors of this study note that the source of racial and ethnic disparities in the prescribing of medication to treat mental disorders requires further study. The absence of independent diagnostic data prevents the authors of this study from evaluating the

quality of the prescribing practices. Moreover, further study must also address medication usage in the treatment of nonpsychiatric disorders. The practice of combining psychotropic medications from several classes also warrants further research for better understanding of the significance of this trend.

Table 2

What a Parent/Caregiver Needs to Know about their Child and Antidepressant Use

- Be clear and honest when talking with your child about the possible risks and benefits of taking an antidepressant medication.
- Talk to your child or adolescent about whether they are having any suicidal thoughts, and let them know they should come to you immediately if they start having suicidal thoughts or any other troubling symptoms while they are taking antidepressant medication.
- Working with your child and your child's physician, you should develop a "safety/crisis plan" for your child. This can include identifying an adult your child can call if he/she is thinking about suicide.
- You and your child's physician should closely monitor your child - especially during the first months of treatment. Any child or adolescent starting an antidepressant medication should be followed weekly (in person or by telephone) for the first month, every other week (preferably in person) for the second month, and at least once a month (in person) thereafter by the treating physician to check for the severity of depressive symptoms, suicidal behavior and any other problems.
- It is important that you do not suddenly stop or change the dose of your child's antidepressant medication without first talking to your child's physician.

Source: New York State Office of Mental Health, 2004.

Conclusion

Controversy regarding the use of antidepressants in children and adolescents continues. As stated above, there is a need for further study of antidepressant use in children and adolescents to address the concerns outlined in the FDA advisory. The AMA has asserted that its review of various studies supports the view that antidepressants reduce suicidal behavior and completed suicide attempts overall (2005). The organization does acknowledge, however, that the risk of such behavior appears to be highest during the initial course of drug therapy. Its position is that antidepressants should continue to be available, with their use guided by sensible clinical judgment (AMA). The decision-making regarding the treatment of a child or adolescent patient must ultimately address all the circumstances and symptoms that are present in the patient, as well as their family supports and the diagnostic and treatment resources available to both families and clinicians (AMA).

Sources

American Academy of Child & Adolescent Psychiatry (AACAP). (2000). Psychiatric Medication for Children and Adolescents Part II: Types of Medications. *American Academy of Child & Adolescent Psychiatry Facts for Families 29*. [Online]. Available: http://www.aacap.org/publications/factsfam/29.htm. [July 2005].

American Medical Association (AMA). (2005). Safety and Efficacy of SSRIs in Children and Adolescents (A-05). *Council on Scientific Affairs*. [Online]. Available: http://www.ama-assn.org/ama/pub/category/15186.html. [July 2005].

Bridge, J., Iyengar, S., Salary, C., Barbe, R., Birmaher, B., Pincus, H., Ren, L., & Brent, D. (2007). Clinical Response and Risk for Reported Suicidal Ideation and Suicide Attempts in Pediatric Antidepressant Treatment: A Meta-analysis of Randomized Controlled Trials. *Journal of the American Medical Association. 297*, 1683-1696.

DeNoon, D. (2004). Child Antidepressant Use Skyrockets Use Growing Fastest in Preschool Kids. *Web MD Medical News*. [Online]. Available: http://my.webmd.com/content/article/85/98399.htm. [July 2005].

Friedman, R., & Leon, A. (2007). Expanding the Black Box—Depression, Antidepressants, and the Risk of Suicide. *The New England Journal of Medicine, Volume 356* (23), 2343-2346. [Online]. Available: http://content.nejm.org/cgi/content/full/356/23/2343. [January 2008].

Gibbons, R., Hur, K., Bhaumik, D., & Mann, J. (2006). The Relationships between Antidepressant Prescription Rates and Rate of Early Adolescent Suicide. *American Journal of Psychiatry*, *163*, 11, 1898-1904.

Jancin, B. (2005). Toxicology Shows Antidepressants Present in 21% of Suicide Completers. *Clinical Psychiatry News, 33 (6)*, 6.

Lock, J., Walker, L., Rickert, V., & Katzman, D. (2005). Suicidality in Adolescents Being Treated with Antidepressant Medications and the Black Box Label: Position Paper of the Society for Adolescent Medicine. *Journal of Adolescent Health, 36*, 92-93.

National Institute of Mental Health (NIMH). (2008). *Antidepressant Medications for Children and Adolescents: Information for Parents and Caregivers*. [Online]. Available: http://www.nimh.nih.gov/health/topics/child-and-adolescent-mental-health/antidepressant-medications-for-children-and-adolescents-information-for-parents-and-caregivers.shtml. [January 2008].

New York State Office of Mental Health. (2004). OMH Letter to Facilities and Programs Concerning Antidepressant Use in Children and Adolescents. [Online]. Available: http://www.omh.state.ny.us/omhweb/advisories/parentltr.htm. [July 2005].

Olfson, M., Marcus, S., & Shaffer, D. (2006). Antidepressant Drug Therapy and Suicide in Severely Depressed Children and Adults. *Archives of General Psychiatry, 63*, 865-872.

Olfson, M., Marcus, S., Weissman, M., & Jensen, P. (2002). National Trends in the Use of Psychotropic Medications by Children. *Journal of the American Academy of Child & Adolescent Psychiatry, 41(5)*, 514-521.

Reuters Health Information. (2005). U.S. Youth Antidepressant Use Drops in 2004-Report. [Online]. Available: http://www.medscape.com/viewarticle/498607_print. [February 2005]. *Not Available July 2005.*

Simon, G., Savarino, J., Operskalski, B., & Wang, P. (2006). Suicide Risk during Antidepressant Treatment. *American Journal of Psychiatry, 163 (1)*, 41-47.

U.S. Food and Drug Administration (FDA). (2004). FDA Public Health Advisory: Suicidality in Children and Adolescents Being Treated with Antidepressant Medications. [Online]. Available: http://www.fda.gov/cder/drug/antidepressants/SSRIPHA200410.htm. [July 2005].

U.S. Food and Drug Administration (FDA). (2007). FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications. [Online]. Available: http://www.fda.gov/bbs/topics/NEWS/2007/NEW01624.html. [January 2008].

Virginia Joint Commission on Health Care. (2005). Decision Matrix.

Wolf, D. (2005). Suicidality Following Black-Box Warning–Letters to the Editor. *Journal of the American Academy of Child & Adolescent Psychiatry, 44(5)*, 405.

Additional Resources

American Academy of Child & Adolescent Psychiatry (AACAP)
Children and Psychiatric Medications
http://www.aacap.org/publications/childMed

Cuffe, S. (2004). *Do Antidepressants Increase the Risk of Suicide in Children and Adolescents?* American Academy of Child & Adolescent Psychiatry (AACAP) DevelopMentor.
http://www.aacap.org/training/DevelopMentor/Content/2004Fall/f2004_a2.cfm

March, J., Silva, S., Petrycki, S., & the Treatment for Adolescents with Depression Study (TADS) Team. (2004). Fluoxetine, Cognitive Behavioral Therapy, and a Combination for Adolescents with Depression: Treatment for Adolescents with Depression Study (TADS) Randomized Controlled Trial. *Journal of the American Medical Association, 292*, 807-820.

MayoClinic.com
Children and Antidepressants: Sorting through the Warnings
http://www.mayoclinic.com/invoke.cfm?id=MH00059

National Institute of Mental Health (NIMH)
Report on the Treatment of Children with Mental/Emotional Disorders; Includes Sections on Medications and Other Treatments; Info on Commonly Prescribed Psychotropic Medications, Side Effects, and the Approved Ages for Prescriptions.
http://www.nimh.nih.gov/publicat/childqa.cfm

National Mental Health Association
Antidepressant Medication and Children: Tips for Parents
http://www.nmha.org/infoctr/factsheets/antidepressantsChildrenTips.cfm

New York University Child Study Center
Guide to Psychiatric Medications for Children and Adolescents
http://www.aboutourkids.org/aboutour/articles/guidetopsychmeds.html

ParentsMedGuide
The Use of Medication in Treating Childhood and Adolescent Depression: Information for Patients and Families
http://www.parentsmedguide.org/parentsmedguide.htm

U.S. States Food and Drug Administration (FDA)
Proposed Medication Guide to Using Antidepressants in Children or Teenagers
http://www.fda.gov/cder/drug/antidepressants/SSRIMedicationGuide.htm.

Organizations/Weblinks

American Academy of Child & Adolescent Psychiatry (AACAP)
3615 Wisconsin Avenue, N.W. - Washington, DC 20016-3007
202-966-7300
http://www.aacap.org

American Academy of Pediatrics (AAP)
141 Northwest Point Blvd. - Elk Grove Village, IL 60007-1098
847-434-4000
http://www.aap.org

American Counseling Association
5999 Stevenson Avenue - Alexandria, VA 22304-3300
800-347-6647; TDD 703-823-6862
http://www.counseling.org

American Psychological Association (APA)
750 First Street, N.E. - Washington, DC 20002-4242
800-374-2721
http://www.apa.org

Center for Healthier Children, Families, and Communities
1100 Glendon Ave., Suite 850 - Los Angeles, CA 90024
310-794-2583
http://healthychild.ucla.edu

The Child Trauma Academy
5161 San Felipe, Suite 320 - Houston, TX 77056
713-818-3967
http://www.childtrauma.org

National Institute of Mental Health (NIMH)
Treatment of Children with Mental Disorders
6001 Executive Blvd. - Room 8184, MSC 9663 - Bethesda, MD 20892-9663
301-443-4513
http://www.nimh.nih.gov

National Mental Health Association (NMHA)
1021 Prince Street - Alexandria, VA 22314-2971
800-969-NMHA (6642)
http://www.nmha.org